Message

From: White, Paul [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=4E179825823C44EBBB07A9704E1E5D16-WHITE, PAUL]
Sent: 11/15/2019 2:04:10 PM
To: Schlosser, Paul [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=121cf759d94e4f08afde0ceb646e711b-Schlosser, Paul]; Jerry Campbell [JCampbell@ramboll.com]; Harvey Clewell [HClewell@ramboll.com]; Robinan Gentry [rgentry@ramboll.com]
CC: Walsh, Patrick [patrick-walsh@denka-pe.com]; Thayer, Kris [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=3ce4ae3f107749c6815f243260df98c3-Thayer, Kri]; Cascio, Wayne [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a1bd931ca2f84ea8ac2f4c44538f3589-Cascio, Wayne]; Jones, Samantha [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=eac77fe3b20c4667b8c534c90c15a830-Jones, Samantha]; Lavoie, Emma [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=86ac7844f12646c095e4e9093a941623-Lavoie, Emma]; Bahadori, Tina [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=7da7967dcafb4c5bbc39c666fee31ec3-Bahadori, Tina]; Kirby, Kevin [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=cbb65672f6f34545be460a66ff6fa969-Kirby, Kevin]; Vandenberg, John [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=dcae2b98a04540fb8d099f9d4dead690-Vandenberg, John]; Morozov, Viktor [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=03cc9abb639c453fabc2bbb3e4617228-Morozov, Viktor]; Davis, Allen [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=a8ecee8c29c54092b969e9547ea72596-Davis, Allen]; Hawkins, Belinda [/o=ExchangeLabs/ou=Exchange Administrative Group (FYDIBOHF23SPDLT)/cn=Recipients/cn=075561d171e845828ec67a945663a8e6-Hawkins, Belinda]
Subject: RE: Chloroprene PBPK: sensitivity analysis scripts

Paul,
You are putting in a major effort here, and for my part want to express thanks! I hope all appreciate the amount of work and careful attention to detail that goes into this evaluation.

Paul W.

From: Schlosser, Paul <Schlosser.Paul@epa.gov>
Sent: Friday, November 15, 2019 8:48 AM
To: Jerry Campbell <JCampbell@ramboll.com>; Harvey Clewell <HClewell@ramboll.com>; Robinan Gentry <rgentry@ramboll.com>
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Subject: RE: Chloroprene PBPK: sensitivity analysis scripts

Jerry,

Yes, I've been updating the scripts to just use name indexing, but my practice is to start by running a script as-is, and the resulting SCs were very different from those shown in the report figures. I rechecked that my version of Figure 7 wasn't using a wrong-# index, but that used "AMPLU".

I think the only output I still need to check are results in the table on p. 21 of the main report (just for the current model), but then I need to document everything, make sure I've checked all parameters in the code vs. the report tables vs. the spreadsheets.

-Paul

From: Jerry Campbell <JCampbell@ramboll.com>
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Subject: RE: Chloroprene PBPK: sensitivity analysis scripts

Paul,

Ok, I thought that might be the case after I noticed the difference in our two output list.

Regarding the SA files: Per our discussion last week, I have modified my SA scripts so they now call the variable by the string value rather than the column number and pull the parameter values for the SA loop based on the string value of the parameter rather than putting the parameter list in the file directly. It was a good suggestion that will avoid issues in the future when variable list or parameter values might be altered in the future. I'd suggest that you follow that paradigm rather than using the column number. In this case the column number would be replaced by "AMPLU" or "CV" instead of current column numbers 24 or 20 (CV location in your matrix). I had made changes to the base model parameterization based on your suggested changes as we've gone along and I didn't want to send any revised files until it had been QC'd on our end and we'd written a response to your suggested changes. Otherwise, there would be no record of what we'd discussed to ease any final checks you wanted to run. None of the changes will alter the sensitive parameters as the structure of the model and underlying parameterization are essentially still the same.

Just for the record: I have moved CV in my output list to the same position as yours. It makes more sense to put it there rather than the end but I didn't want to alter the output order at the time as you were already QA'ing the model. It won't matter with the revised scripts as we avoid this issue.

As a side, I have also updated all other simulation files that used column number to pull information from the output matrix using the string values for the variable.

Jerry Campbell

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Subject: RE: Chloroprene PBPK: sensitivity analysis scripts

Jerry,

Ah. As part of the discussion/evaluation of which model variable should be compared to the in vivo PK blood data, I added CV to the output list, didn't consider that it would disrupt the numbering in other scripts. So, having updated the scripts accordingly, the SAs were reproduced.

-Paul

From: Jerry Campbell <JCampbell@ramboll.com>
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Subject: RE: Chloroprene PBPK: sensitivity analysis scripts

Paul,

Where did you acquire the "chloroprene.model" file with CV as the 20th variable in the output list? It's not the 20th variable in the version that I uploaded for QA and I don't have a record of sending you a revised model file with CV as the 20th item.

Jerry Campbell

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Subject: Chloroprene PBPK: sensitivity analysis scripts

Jerry,

In the Fmouse_Metric_SA.R and Human_continuous_SA.R scripts, the output variable being captured, # 23, is the liver metabolic intensity, AMP, not the lung (# 24, AMPLU).

```
> out[1,]<-1:28
> out[1,]
  time     AI     AX     AM   AMLU    AMK    ALU     AL     AK     AS     AR     AF
     1      2      3      4      5      6      7      8      9     10     11     12
MASBAL    CLU     CL     CK     CS     CR     CF     CV  CVLUM    ppm    AMP  AMPLU
    13     14     15     16     17     18     19     20     21     22     23     24
  AMPK    cvl  qcbal   vbal
    25     26     27     28
```

I assume the values in the spreadsheet (with plots) where from the acslX version, as once I make this correction in the SA scripts the resulting SC values are almost the same, only off by 0.01 in a few cases, and are identical for the human SC values.

Similar to what I did for the mouse_inviv_SA script, I've condensed these SA scripts and put the human metabolic parameters into params/Human.R file, to facilitate the QA.

?? Do you have a spreadsheet where Figure 8 is created?

-Paul

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